Disseminated Tuberculosis

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ABSTRACT

Tuberculosis is one of 6 fatal infectious diseases in the world, and causes three million deaths annually. Tuberculosis (TB) is a pulmonary and systemic disease caused by Mycobacterium tuberculosis. TB classification consists of pulmonary and extra-pulmonary TB. TB stimulates both the specific and non-specific immune systems. Disseminated tuberculosis is milliary lung TB with several extra-pulmonary organ manifestations. The main management for multi-organ TB is the administration of anti-tuberculosis drugs. In pleural effusion due to lung TB, corticosteroid may reduce systemic and local reactions to tuberculoprotein, reduce pleural exudate secretion and fibrosis, as well as reduce deformity of the chest wall and scoliosis that can inflict children.

We report a case of a 25 year-old woman who came with a chief complaint of progressive breathing difficulty since 2 days prior to admission. Since 1 year prior to admission, the patient's abdomen became bloated and there was edema in her legs. Her lost her appetite and weight, and suffered from a mild fever. The patient had a cough with thick whitish sputum. The patient had not menstruated for 7 months. She had a history of liver disease.

Physical examination results were as follows: the patient was moderately ill, fully conscious, and had malnutrition. She weighed 37 kg and was 149 tall. Her blood pressure was 100/70 mmHg, her pulse rate 84 times/minute, her body temperature 37^0 Celsius, and her respiration rate 18 times per minute. Her conjunctiva were pale. Her right supra-clavicular and mandibular lymph nodes had a diameter of 2 cm, were resilient, mobile, not tender, and had smooth surfaces. Her lung sounds demonstrated weakened vesicular sounds in her left lung, with loud rales in both lungs. Her abdomen was enlarged, distended to 92 cm, with venectations. Her liver and spleen could not be assessed. There was undulation and normal bowel sounds. Her extremities were warm and edematous. Her left inguinal lymph node was enlarged to 1 cm, resilient, well-defined, mobile, and not tender. Her left inguinal lymph node was 5 mm in diameter.

Her laboratory results were as follows: Hemoglobin level 9.0 g/dl, Hematocryte level 27 vol%, erythrocyte count 3.66 juta/ul, and leukocyte count 14.500/ul. Her chest x-ray demonstrated milliary tuberculosis. Abdominal ultrasound revealed a congestive liver, exudative peritonitis, and a mass in the spleen. Ascites fluid aspiration revealed exudate fluid. Pathological cytology revealed chronic granulomatous inflammation, with the possibility of TB, and no signs of malignant cells. Ascites fluid microbiological culture turned out negative. During the first echocardiography, no pericardial effusion was found, and the ejection fraction was 61%. During the second echocardiography, there was thickening of the walls, and pericardial effusion. Catheterization was attempted, but failed due to cyanosis. Electrocardiography demonstrated low voltage at nodes I, II, aVR, aVL, aVF. The patient was consulted to the retina subdivision, and no tubercle was found.

Problem: disseminated TB with pericarditis, ascites due to exudative peritonitis, anemia, malnutrition, and secondary amenorrhea. The patient's condition improved under treatment of RHZE 300/300/1000/750mg, 3x1 tablet of B complex vitamins, 3x10 mg of prednison, 1x100 mg of aldactone, and 1x1 tablet of provera. Her difficulty breathing alleviated, her waist diameter was reduced to 76 cm.

Key words: *Disseminated Tuberculosis, Pericarditis, Ascites*

INTRODUCTION

According to the WHO, tuberculosis is currently one of the 6 main causes of death in the world, and causes more deaths than malaria.[1] There are 6 fatal infectious diseases that make up 90% of the cause of death, pneumonia, diarrhea, measles, tuberculosis, malaria, and HIV/AIDS.

Tuberculosis causes three million deaths annually, which is approximately 6% of all deaths in the world, and is one of ten most common causes of death at a young age.[2]

Tuberculosis is a pulmonary and systemic disease caused by *Mycobacterium tuberculosis*. Currently, Indonesia is the third nation (204, 323 new cases) with the

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greatest number of tuberculosis cases after India and China. The increase in the number of cases occur particularly due to inadequate control and high frequency of *M. tuberculosis* infection and HIV co-infection in various countries.[3]

Tuberculosis is classified into pulmonary and extra-pulmonary tuberculosis. Pulmonary tuberculosis is when *M. tuberculosis* is found in the lungs, while extra-pulmonary tuberculosis is infection of *M. tuberculosis* outside of the lungs. Common sites for extra-pulmonary infection include the pleura, lymph nodes, peritoneum, gastrointestinal tract, urinary tract, and vertebrae. Organs that are rarely infected are the mouth, tongue, eyes, and adrenal glands. Even though tuberculosis most commonly infects the lungs (pulmonary tuberculosis), extra-pulmonary tuberculosis is also an important manifestation, particularly due to currently common *M. tuberculosis* co-infection with HIV infection.[5-7] Prior to the epidemy of HIV infection, almost 85% of tuberculosis cases were pulmonary, while 15% were extra-pulmonary or both. After the HIV epidemy, only 38% cases are localized in the lungs, while 30% were extra-pulmonary, and 32% was a combination of both.[8] As many as 33% of tuberculosis multi-organ infection was found among HIV patients.[9,10] The extent of tuberculosis in HIV patients was also found in patients with limited immune function, who were thus unable to localize *M. tuberculosis* infections. This category of patients includes children under 5 years of age, elderly patients, and patients with primary or secondary immunodeficiency due to other diseases or malnutrition.[9] Tuberculosis stimulates both specific and non-specific immune systems. At this moment, cellular immunity, particularly T cell CD4, is known to be the main T cell responsible for the regulation of the immune system against *M. tuberculosis*. This cell plays a role in inducing and assisting the immune system in recognizing antigens, and plays a role in increasing the immune response by secreting various lymphokines, and together with CD8 cells causes lysis of target cells. The lymphokines that are then produced activate the phagocytosis of mononuclear cells to control the growth of intracellular microbacterium.[11]

Disseminated tuberculosis is milliary pulmonary tuberculosis with manifestations on several extra-pulmonary organs. A patognomonic sign of disseminated tuberculosis is the presence of choroids tubercles, a granuloma located in the choroids.[12] Disseminated and milliary tuberculosis occurs due to the body's inability to localize *M. tuberculosis* infection due to HIV infection or other immunodeficiencies. Clinical manifestations are usually unspecific and are dominated by systemic symptoms such as fever, weight loss, anorexia, and fatigue. Other symptoms usually depend on the target organ. Tuberculin tests in disseminated tuberculosis rarely produce positive results compared to other types of tuberculosis infection.

The main management for multi-organ tuberculosis is the administration of Anti-tuberculosis agents. In cases of pleural effusion due to pulmonary tuberculosis, corticosteroids may reduce systemic and local symptoms due to a reaction towards tuberculoprotein, reduce pleural exudation and fibrosis, and reduce deformity of the chest wall and scoliosis that may occur in children.

CASE REPORT

A patient, Mrs. S. was hospitalized with a chief complaint of difficulty breathing that worsened since 2 days prior to admission.

Since 1 year prior to admission, the patient's abdomen and both legs had swelled. The patient had been hospitalized at a Tangerang Hospital and was said to have liver disease, and received treatment of lesichol (3x1), 1x100 mg of aldactone, 1x300 mg of rifampicin, 3x150 mg of ethambutol, and 2x500 mg of pyrazinamid for 5 months. The patient's weight and appetite dropped, and there was subfebrile fever.

Since 3 months prior to admission, the patient complained of cough with white mucoid sputum and a fluctuating fever, accompanied by night sweats, and occasional difficulty breathing. The patient had stopped menstruating (prior to the time, her menstruation was regular).

She denied prior heart disease. The patient suffered from liver disease when she was in primary school.

From physical examination, we found the patient to be moderately ill, fully conscious, and malnutritious. The patient weighed 37 kg, was 149 cm tall, had a blood pressure of 100/70 mmHg, a pulse rate of 84 times/minute, a body temperature of 37° Celsius, and a respiratory rate of 18 times/minute. Her conjunctiva were pale, her sclera was not icteric, her jugular venous pressure was 5-2 cmH_2O. Her right supraclavicular and mandibular lymph nodes were palpable, and mobile, with a diameter of 2 cm, smooth edges, and no tenderness. Her first and second heart sounds were pure, without murmur or gallop. Her lungs were symmetrical in static and dynamic conditions, her fremitus were symmetrical, vesicular sounds of the left was weakened, and there was loud rales on both lungs, without wheezing. Her abdomen was distended to a waist diameter of 92 cm, stretched, with venectations. Her liver and spleen were difficult to asses. There was undulation, and normal bowel sounds. Her

extremities were warm, and there was edema. Her left inguinal lymph node was enlarged, pliant, limited, and mobile, with a diameter of 1 cm and no tenderness. The right inguinal lymph node was 0.5 cm in diameter.

Laboratory results were as follows: Hemoglobin level 9.0 g/dl, Hematocryte 27 vol%, erythrocyte count 3.66 million/ul, leukocyte count 14,500/ul, platelet count 210 thousand/ul, ureum level 22 mg/dl, creatinine level 0.8 mg/dl, blood glucose 68 mg/dl. Chest x-ray demonstrated milliary tuberculosis.

In this patient, the following problems were established: milliary pulmonary tuberculosis, ascites, anemia, and malnutrition. Pulmonary tuberculosis was determined based on long-standing cough with fluctuating fever, night sweats, and weight loss. During physical examination, we found loud rales in both lungs, enlarged lymph nodes, and findings of milliary tuberculosis from the chest x-ray, with a possibility of constrictive pericarditis. The patient was scheduled to undergo the following diagnostic procedures: 3x sputum acid-fast bacilli assessment, tuberculin test, LED, and echocardiography. Plans for treatment are as follows: RHZE (1x 300 mg of Rifampizin, 2 x 500 mg of Pirazinamide, 3 x 250 mg of Ethambutol).

Ascites in this patient was determined based on a distended abdomen with positive undulation, believed to be due to peritonitis tuberculosis, with the possibility of chronic liver disease and a differential diagnosis of hypoalbuminemia. Diagnostic plans were for liver function tests of SGOT, SGPT, and CHE; abdominal ultrasound, puncture and analysis of ascitic fluid. The patient was treated with 1x100 mg of aldactone.

Anemia was established based on pale conjuctivas and a hemoglobin level of 9.0 g/dl. It is thought to be due to chronic disease, even though other possibilities had not been excluded. The diagnostic plans at the time were serial complete peripheral blood tests, erythrocyte morphology, serum iron, and TIBC.

Malnutrition was established based on a bodyweight of less than 90% of the ideal body weight. The patient weighed 37 kg and was 149 cm tall. This condition was thought to be due to chronic disease. Diagnostic plans were to monitor bodyweight and conduct albumin evaluation. Plans for treatment were administration of a high calorie high protein diet and consultation with the nutrition department.

On the third day of treatment, abdominal ultrasound found liver congestion, exudative peritionitis, and mass in the spleen. The patient was consulted to the department of obstetrics and gynecology for the possibility of cystoma. No cystoma was found, but there was secondary amenorrhea, and the patient was advised to get 1x1 tablets of provera. The patient underwent aspiration of ascites fluid, resulting in exudates fluid. Pathologic cytology assessment concluded findings of chronic granulomatous inflammation, with the possibility of tuberculosis, while no malignant cells were found. Microorganism culture of the ascites fluid turned out negative.

The patient was scheduled to undergo echocardiography. The results of echocardiography found no signs of pericardial effusion, with an ejection fraction of 61%. Based on rounds from the cardiac subdivision in the ward, it was concluded that the echocardiography was hard to assess, and thus a repeated echocardiography was rendered necessary. The second echocardiography demonstrated thickening of the walls, and pericardial effusion. The patient also underwent catheterization, but it failed due to cyanosis. Electrocardiography demonstrated low voltage at I, II, aVR, aVL, and aVF. The patient was consulted to the subdivision of retina for the possibility of ocular tubercles. In this patient, no ocular tubercle was found.

The patient's problems were then revised into disseminated tuberculosis with pericarditis, ascites due to exudative peritonitis, anemia, malnutrition, and secondary amenorrhea.

During treatment, the patient's clinical condition improved. There was no more difficulty breathing, and the patient's waist diameter dropped from 92.5 cm to 76 cm. The treatment that was administered was as follows: RHZE (1x 300 mg of Rifampizin, 2 x 500 mg of Pirazinamide, 3 x 250 mg of Ethambutol), 3 x 1 tablets of B complex, 3 x 10 mg of prednisone for 2 weeks followed by tapering off, 1 x 100 mg of aldactone, and 1 x 1 tablet of provera.

DISCUSSION

This is a case of disseminated tuberculosis, where pulmonary findings demonstrated milliary tuberculosis accompanied by extra-pulmonary tuberculosis. Disseminated tuberculosis was established based on clinical findings, chest x-ray, abdominal ultrasound, and analysis of ascites fluid. Triple sputum acid-fast bacilli assessment demonstrated positive results. Consultation with the ophthalmology department did not demonstrate the presence of ocular tubercles. The possibility of tuberculous peritonitis as a form of extra-pulmonary tuberculosis in this patient is high, and abdominal ultrasound demonstrated exudative peritonitis.

In this patient, there was disseminated tuberculosis complicated by exudative pleuritis and pericarditis, where

pericarditis is rarely found, and when found, there are usually signs of idiopathic cardiomegaly or heart failure or arrhythmia.

Calcification of the pericardium found in chest x-ray is usually a strong support from the diagnosis, but in this patient, this was not found. The patient was scheduled for heart catheterization to establish the diagnosis of constrictive pericarditis, but clinical findings did not allow treatment until the patient left on her own will after 2 months treatment.

Steroid treatment in this patient was particularly aimed for tuberculosis peritonitis. It is hoped that administration of steroids (3x2 tablets of Prednison) for 2 weeks followed by tapering off, would facilitate absorption of ascites fluid. The results of treatment were very good, where subjective complaints and objective examinations demonstrated clinically significant improvements, and improved appetite. The patient's bodyweight increased to 39.5 kg.

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